



State of California—Health and Human Services Agency  
**Department of Health Care Services**



Edmond G. Brown Jr  
Governor

June 7, 2012

Number Letter: 03-0512  
Index Benefits

TO: ALL COUNTY CALIFORNIA CHILDREN SERVICES (CCS) PROGRAM  
ADMINISTRATORS, MEDICAL CONSULTANTS, AND STATE  
CHILDREN'S MEDICAL SERVICES (CMS) AND GENETICALLY  
HANDICAPPED PERSONS PROGRAM (GHPP)

SUBJECT: IVACAFITOR (KALYDECO™)

## **I. PURPOSE**

The purpose of this Numbered Letter (NL) is to establish CCS and GHPP policy regarding the authorization of Ivacaftor, as a treatment for cystic fibrosis (CF) due to G551D mutation in the CF transmembrane conductance regulator (CFTR) gene. Ivacaftor is the first of a new class of drugs known as potentiators, and has been associated with significant clinical improvement in individuals with one or two copies of the G551D mutation.

## **II. BACKGROUND**

CF is a life-threatening recessive genetic disease affecting respiratory and digestive systems. In California, CF is found in all race/ethnic groups at a prevalence of around 1/3,500 in non-Hispanic whites, 1/7,900 in Hispanic whites, 1/8,000 in non-Hispanic blacks, and 1/23,500 in Asians and others. CF caused by a defective gene for the CFTR protein. Defective CFTR results in decreased secretion of chloride and increased reabsorption of sodium and water across epithelial cells. This leads to viscous (sticky) secretions, which are harder to clear and increase susceptibility to life-threatening pulmonary infections. In addition, the viscous secretions obstruct the release of pancreatic enzymes, leading to malabsorption of food.

Standard therapies for CF target amelioration of symptoms and prevention of infection. Ivacaftor on the other hand, targets the pathology of the disease. In individuals with the G551D mutation (2-4 percent of those with CF, Ivacaftor binds to the defective receptor, and facilitates passage of chloride ions across the defective CFTR, normalizing the secretions. Its efficacy over 48 weeks was demonstrated in a Phase III trial of individuals 12 years and older, in which there were 55 percent fewer exacerbations, pulmonary lung

function scores (FEV1) with improvement by an average of 10 percent, and better quality of life.

Additional trials extending this study to 60 weeks, and with children ages 6–11, found sustained improvement in lung function. On January 31, 2012, the Food & Drug Administration approved Ivacaftor for use in persons age 6 and over with CF who have the G551D mutation. The recommended dose is 150mg every 12 hours for adult and pediatric (6 years and older) patients.

### **III. POLICY**

Effective the date of this letter, Ivacaftor is a CCS/GHPP benefit when:

- A. Prescribed by a CCS/GHPP approved pulmonology center physician, and
- B. For a CCS/GHPP client with CF with the G551D mutation (defined in III.D. below) whose care is under the supervision and monitoring of a CCS/GHPP approved Cystic Fibrosis and Pulmonology Center, and
- C. For a client 6 years of age or older, and
- D. The request includes documentation of genetic testing at a U.S. laboratory confirming presence of one or two copies of the G551D mutation (e.g., G551D/G551D, F508del/G551D, W1282X/G551D, 1288insTA/G551D, G542X/G551D, R553X/G551D, 621+1G>T/G551D, 711+1G>T/G551D, 1717-1G>A/G551D, 3849+10kbC>T/G551D, dell507/G551D, 2183delAA>G/G551D, R117H/G551D, Y1092X/G551D, 2789+5G>A/G551D, E60X/G551D, R1158X/G551D, G551D/other mutation(s), and G551D/second mutation not identified; the order of the reported mutations is not important), and
- E. Request is submitted with the following baseline parameters (within 6 months) before starting Ivacaftor) and prior to initial authorization:
  - 1. FEV1
  - 2. Weight (and/or BMI)
  - 3. Sweat Chloride
  - 4. Symptom Record

### **IV. POLICY IMPLEMENTATION**

- A. Ivacaftor (Kalydeco™) requires separate authorization.

- B. All requests shall be reviewed by a CCS County Medical Director or designee before authorization of Ivacaftor.
- C. Initial Authorization:
  - 1. Shall be for a 60-day trial.
  - 2. Prior to authorization, documentation must be submitted showing positive genetic test for G551D in the CFTR gene using a testing method that can detect the G551D mutation. All commercial CFTR mutation testing in use today in the U.S. can detect the G551D mutation, except those that specifically test for the F508 del mutation only.
- D. Extensions of the initial authorization shall be granted:
  - 1. When documentation is submitted by the CCS/GHPP approved pulmonary special care center demonstrating at least one of the following after 60 days of Ivacaftor:
    - a. Improvement in FEV1 from baseline by at least 5 percent.
    - b. Reduction in sweat chloride from baseline by at least 5 percent.
    - c. Improvement in Symptom Record from baseline.
    - d. Appropriate weight gain/improvement in nutritional status.
  - 2. For a six-month period or until program eligibility end date, whichever is shorter.
- E. The following shall be considered when reviewing requests for Ivacaftor:
  - 1. Documentation of the presence of only an F508del ( $\Delta$ F508) mutation in the CFTR gene is not medical justification for use of Ivacaftor, as Ivacaftor is not effective in individuals with two copies of the F508del CFTR mutation (i.e., F508del/F508del).
  - 2. Ivacaftor is not a replacement for conventional adjunctive therapy.
  - 3. At this time, the manufacturer recommends not crushing or splitting the tablets. The tablets should be swallowed whole.
- F. Exceptions will be reviewed on a case-by-case basis by State CCS Medical Director or designee.

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If you have any questions regarding this numbered letter, please contact Jill Abramson, MD., State CCS Medical Consultant at (916) 327-2108.

Sincerely,

**Original Signed by Robert Dimand, .M.D.**

Robert Dimand, M.D.  
Chief Medical Officer  
Children's Medical Services